

From the INTERNATIONAL BUREAU

PCT**NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)**

(PCT Rule 44bis.1(c))

To:

CONN, David, L.
Borden Ladner Gervais LLP
World Exchange Plaza
100 Queen Street, Suite 1100
Ottawa, Ontario K1P 1J9
CANADA

Date of mailing (*day/month/year*)

14 September 2006 (14.09.2006)

Applicant's or agent's file reference

PAT2786W-90

IMPORTANT NOTICE

International application No.

PCT/CA2005/000323

International filing date (*day/month/year*)

02 March 2005 (02.03.2005)

Priority date (*day/month/year*)

02 March 2004 (02.03.2004)

Applicant

MCGILL UNIVERSITY et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Athina Nickitas-Etienne

Facsimile No. +41 22 338 82 70

e-mail: pt04@wipo.int

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | |
|--|--|--|
| Applicant's or agent's file reference PAT2786W-90 | FOR FURTHER ACTION | See item 4 below |
| International application No. PCT/CA2005/000323 | International filing date (<i>day/month/year</i>) 02 March 2005 (02.03.2005) | Priority date (<i>day/month/year</i>) 02 March 2004 (02.03.2004) |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | |
| Applicant McGILL UNIVERSITY | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

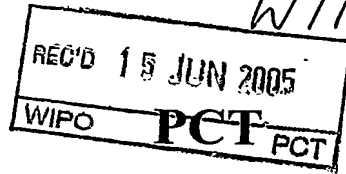
- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

| | |
|--|--|
| <p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p> | <p>Date of issuance of this report 05 September 2006 (05.09.2006)</p> <hr/> <p>Authorized officer Athina Nickitas-Etienne</p> <p>e-mail: pt04@wipo.int</p> |
|--|--|

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY



WIPO

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:
BORDEN LADNER GERVAIS LLP
World Exchange Plaza
1100 - 100 Queen Street
OTTAWA, Ontario
Canada, K1P 1J9

Date of mailing 06 June 2005 (06.06.2005)
(day/month/year)

Applicant's or agent's file reference
PAT2786W-90

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/CA2005/000323

International filing date (day/month/year)
02 March 2005 (02-03-2005)

Priority date (day/month/year)
02 March 2004 (02-03-2004)

International Patent Classification (IPC) or both national classification and IPC
A61K 31/167 A61P 29/00 A61P 11/00 A61P 31/00

Applicant
MCGILL UNIVERSITY ET AL

1. This opinion contains indications relating to the following items :

- | | |
|--|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the opinion |
| <input checked="" type="checkbox"/> Box No. II | Priority |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement. |
| <input type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
Place du Portage I, C114 - 1st Floor, Box PCT
50 Victoria Street
Gatineau, Quebec K1A 0C9
Facsimile No.: 001(819)953-2476

Authorized officer

Tania Nish (819) 934-3592

International application No.
PCT/CA2005/000323

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[] This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :
 - a. type of material

[] a sequence listing

[] table(s) related to the sequence listing
 - b. format of material

[] in written format

[] in computer readable form
 - c. time of filing/furnishing

[] contained in the international application as filed.

[] filed together with the international application in computer readable form.

[] furnished subsequently to this Authority for the purposes of search.
3. [] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments :

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2005/000323

Box No. II Priority

1. ☒ The following document has not yet been furnished :

☒ copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary :

The priority document pertaining to the present application has not been checked as it was unavailable at the time of establishing this first written opinion. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is incorrect, the document, WO 2004/064823 A1, cited in the international search report could become relevant in assessing whether claims 1-5 meet the criteria set forth in Article 33(2-4) PCT.

**International application No.
PCT/CA2005/000323**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2005/000323

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|--------|------------|-----|
| Novelty (N) | Claims | | YES |
| | Claims | <u>1-5</u> | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | <u>1-5</u> | NO |
| Industrial applicability (IA) | Claims | | YES |
| | Claims | | NO |

2. Citations and explanations :

D1: CA 2 365 290 A1
D2: WO 01/72701 A1
D3: Am. J. Respir. Cell Mol. Biol., 22, 460-468
D4: WO 00/00207 A1
D5: J. Biol. Chem., 277, 49531-49537
D6: JNCL, 91, 1138-1146
D7: WO 2004/0644823 A1

NOVELTY

1) D1 discloses the use of ceramides, derivatives and/or precursors of ceramides in the treatment of cystic fibrosis and associated diseases and illnesses, such as inflammation and respiratory infection.

D2 discloses the use of ceramide and derivatives thereof in the prevention of cellular proliferation, inflammatory disease or inflammation.

Therefore, since the subject matter of claims 1-2 and 4-5 is the same as the subject matter disclosed by D1 and D2, claims 1-2 and 4-5 would not be considered novel with respect to D1 and D2. (Art.33(2), PCT)

2) D3 discloses the use of ceramides and analogs thereof in the mediation of cell death by apoptosis. Ceramide is disclosed as a second messenger in initiating the apoptotic response.

D4-D6 disclose the use of fenretinide and other such retinoic acid derivatives in the treatment of hyperproliferative disorders by manipulation of the ceramide-mediated apoptosis.

Therefore, since the subject matter of claim 3 is the same as the subject matter disclosed by D3-D6, claim 3 would not be considered novel with respect to D3-D6 (Art.33(2), PCT)

INVENTIVE STEP

One skilled in their art with regards to D1-D6 would be able to conclude that the increase of ceramide levels will inhibit inflammation and proliferation and thus use of a medicament that increases ceramide levels, such as fenretinide and other like retinoic acid derivatives and precursors/derivatives of ceramide, will treat inflammation and proliferation. (Art. 33(3), PCT)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/CA2005/000323

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 1-5 do lack clarity and conciseness and do not comply with Article 6 (PCT) for the following reasons:

- 1) Claims 1-5 defines the compound used in the treatment as "an agent that increases ceramide levels in the cell". The definition attempts to define the therapeutic compound of the invention solely by the result to be achieved, i.e. the increase of ceramide levels in the cell. Therefore rendering the claims unclear, as it directs to a desired results rather than to the combination necessary to achieve the result as described in the description.
- 2) Claims 1-2 and 4-5 define the use of an agent to treat inflammatory response, proliferation and reduction of respiratory tract infections. The description specifically supports the treatment of respiratory inflammation, proliferation and respiratory infection in subjects with cystic fibrosis (CF) disease using a specific agent, namely fenretinide. Therefore, the claims are broader than the scope of the invention disclosed in the description.
- 3) The term "diseased cell" in claims 1 and 4 cause the claims to be ambiguous
- 4) Claim 3 defines the use of an agent to induce an inflammatory response in a cell. The claim is broader than the scope of the invention as taught in the description where fenretidine is shown to induce an inflammatory response in cells that are not in a pro-inflammatory response, ie cell which are not stimulated.